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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE		
	Application Number	09/989,674
	Filing Date	Nov. 21, 2001
	First Named Inventor	Gordon L. Woods
	Group Art Unit	1617
	Examiner Name	S. A. Jiang
	Attorney Docket Number	2404-105
Title of the Invention:	Method for Regulating Levels of Zinc, Cadmium and Calcium in Humans and for Diagnosing or Screening for the Risk of Developing, Diseases Associated with Abnormal Levels of Cadmium, Zinc and Calcium	

REQUEST FOR RECONSIDERATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In response to the Office Action mailed May 21, 2002, Applicant requests that the rejections of the claims be reconsidered in view of the following comments.

In the Office Action, claims 20-25 and 61, all of the claims currently pending, were rejected under 35 U.S.C. § 103 (a) as unpatentable over Waalkes (Ref. BC in PTO 1449; hereinafter referred to as Waalkes I) and Waalkes (Ref. BF in PTO 1449; hereinafter referred to as Waalkes II). The examiner characterized both references as disclosing that cadmium is useful in pharmaceutical compositions and in the prevention or reduction of NDEA-induced tumor formation in the mouse liver or lung. The examiner acknowledged that neither reference expressly discloses employing cadmium in a method of balancing the concentration of cadmium in body fluids and tissues of a person suffering from unbalanced levels of cadmium in his body fluids and tissues, nor do they disclose correcting a cadmium deficiency in a human suffering therefrom. She

asserted, however, that it would have been obvious to one of ordinary skill in the art to use cadmium in a method of balancing the concentration of cadmium in body fluids and tissues of a human or in a method of correcting a cadmium deficiency in a human suffering therefrom. More specifically, she asserted that one of ordinary skill in the art would have been motivated to use cadmium to balance the concentration of cadmium in a human's body fluids and tissues and to correct a cadmium deficiency because cadmium is known to be useful in a pharmaceutical composition and in the prevention or reduction of NDEA-induced tumor formation in mice. In view of these teachings, she averred that one would have had a reasonable expectation that the administration of cadmium would have a beneficial therapeutic effect on balancing cadmium concentrations in the body fluids and tissues of humans suffering from unbalanced levels of cadmium and on correcting a cadmium deficiency in humans suffering therefrom. This rejection is traversed.

This Office Action was discussed with the examiner and her supervisor in an interview attended by the inventor and his undersigned representative on August 13, 2002. Applicant and his representative appreciate the opportunity to discuss the application.

As the examiner correctly noted, the cited references do not disclose using cadmium to balance cadmium concentrations in human body fluids and tissues or to correct cadmium deficiencies in humans. Neither do the references, taken individually or in combination, suggest such a use for cadmium. Indeed, the references do not even recognize that humans can suffer from either unbalanced levels or a deficiency of cadmium in their body fluids and tissues. As the references do not recognize the

problems discussed in the present application, much less suggest a means of solving them, the references do not render obvious the presently claimed invention.

Indeed, each of the references, far from recognizing that humans can suffer from a cadmium imbalance or a cadmium deficiency, begins by noting that cadmium "is a non-essential, toxic transition metal" that is a "suspected human carcinogen" and a "highly cytotoxic agent" (Waalkes I, p. 1656), and that cadmium is "a toxic, nonessential transition metal that is classified as a human carcinogen and is a potent animal carcinogen" (Waalkes II, p. 1026). In contrast to these teachings, the premise underlying the Applicant's invention is that cadmium actually is an essential trace metal in humans and that it is a deficiency, rather than the mere presence, of cadmium in the human body that actually is associated with the onset or increased severity of certain diseases or disorders. More specifically, as Applicant teaches beginning on page 11 of his application, it appears that an underlying cause of certain diseases is a deficiency of cadmium which, in turn, leads to an increased urinary excretion of zinc and a secondary zinc deficiency. If cadmium levels in body fluids and tissues are out of balance or deficient, zinc levels also will be out of balance. By the administration of cadmium, levels of cadmium in body fluids and tissues can be brought into balance and cadmium deficiencies can be corrected.

None of this is suggested by the cited references. Indeed, neither Waalkes I nor Waalkes II discusses human treatment at all, although undoubtedly the ultimate purpose of their research is to find a therapeutic agent for administration to humans. The Waalkes papers merely report the results of early animal studies. More specifically, the focus of both Waalkes I and Waalkes II is the administration of

cadmium to mice which have induced liver and lung tumors. In Waalkes I, the authors conclude that cadmium effectively can "impair tumor formation in the male B6C3F1 mouse liver and lung." (page 1659). They also found that cadmium administration could suppress spontaneously occurring tumors in these mice. They note that these results are in apparent conflict with previous studies which indicate that cadmium is a potent carcinogen in rodents in a variety of tissues. They suggest that whether cadmium is carcinogenic or anticarcinogenic appears to be due to a complex set of circumstances that requires further research to define (page 1660). It is clear from a review of the whole paper that Waalkes and his co-authors are reporting preliminary research results--in mice--and that no conclusions can be drawn as to the ultimate role of cadmium as a therapeutic agent. The final sentence in the paper is illustrative: "[t]he potential chemotherapeutic effects of cadmium deserve further study." The authors thus do not set forth any conclusions with regard to their studies in mice, much less discuss the administration of cadmium to humans.

The Waalkes II paper, published three years later, evaluated the results of intravenous administration of cadmium to mice with NDEA-induced tumors. The results confirmed that cadmium effectively can impair tumor formation in male B6C3F1 mouse liver and possibly lung. The authors also reported that metallothionein, a protein associated with tolerance to cadmium, was not detected in mouse liver tumors, although normal liver cells expressed high levels after cadmium exposure. They noted that the effect of cadmium on hepatic tumor incidence and growth appeared to depend on a reduced activity and responsiveness of the metallothionein system in transformed liver cells and that minimal expression of metallothionein in human hepatocellular

tumors might indicate a common sensitivity. They again concluded that the "potential chemotherapeutic effects of cadmium deserve additional study" (page 1032).

Thus, both of these studies raise the possibility that cadmium, on the basis of studies in mice, under certain circumstances, may act as a therapeutic agent, specifically, as an anti-neoplastic agent. This is a far cry from rendering it obvious that humans can suffer from an imbalance of cadmium in their body fluids and tissues which can be corrected through the administration of a cadmium salt or that humans can suffer from a cadmium deficiency which can be corrected through the administration of a cadmium salt.

At the interview, the Patent Office representatives asserted that mice are a good model for the effects of cadmium administration to humans and that, on the basis of the studies described by Waalkes et al., one would expect cadmium to be a useful therapeutic agent in humans. This assertion is completely conclusory, for there is nothing in the record to support it. There is nothing in the record to indicate that mice should be considered a suitable model for humans with regard to cadmium administration for any purpose, nor is there any indication that mice can suffer from a systemic cadmium deficiency or imbalance. Neither of the Waalkes et al. papers provides any information on the systemic cadmium levels of the mice at the beginning of or during the studies, much less whether those levels were typical or atypical of murine cadmium levels. The references fairly provide only that in two specific preliminary studies the administration of cadmium to mice resulted in a decrease in the formation and incidence of specific types of tumors.

Applicant respectfully suggests that the only way in which the examiner could conclude from the teachings of the references that the claimed invention is obvious is to have relied upon hindsight. It is a well accepted tenet of patent law that hindsight is not the correct basis upon which an obviousness determination is to be made. "To imbue one of ordinary skill in the art with the knowledge of an invention ..., when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *Gore v. Garlock,* 220 USPQ 303, 313 (F.Cir. 1983). Applicant respectfully suggests that such hindsight reliance has occurred here and that, accordingly, the rejection should be withdrawn.

Applicant respectfully submits that the claims pending in the application now are in condition for allowance.

<table>
<tr><td colspan="6">☒ Customer Number or Bar Code Label 6449</td></tr>
<tr><td>Name</td><td colspan="5">Barbara G. Ernst, Reg. No. 30,377</td></tr>
<tr><td>Signature</td><td colspan="2">Barbara G Ernst</td><td>Date</td><td colspan="2">October 11, 2002</td></tr>
<tr><td>Address</td><td colspan="5">Rothwell, Figg, Ernst & Manbeck
Suite 701-East, 555 13th Street, N.W.</td></tr>
<tr><td>City</td><td>Washington</td><td>State</td><td>D.C.</td><td>Zip Code</td><td>20004</td></tr>
<tr><td>Country</td><td>U.S.A.</td><td>Telephone</td><td>202-783-6040</td><td>Fax</td><td>202-783-6031</td></tr>
</table>

FEE TRANSMITTAL for FY 2002 (Small Entity)		Complete if Known	
		Application Number	09/989,674
		Filing Date	November 21, 2001
		First Named Inventor	Gordon L. Woods
		Examiner Name	S. A. Jiang
		Group Art Unit	1617
Total Amount of Payment	($) 200.00	Attorney Docket Number	2404-105

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RECEIVED OCT 17 2002 TECH CENTER 1600/2900

METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge additional fees and credit any overpayment to Deposit Account Number 02-2135 in the name of Rothwell, Figg, Ernst & Manbeck

   [X] Charge any Additional Fee Required Under 37 CFR 1.16 and 1.17

   [X] Applicant claims small entity status.

2. [X] Payment Enclosed:
   - [X] Check
   - [ ] Credit Card

FEE CALCULATION

1. FILING FEE

Fee Code	Fee $	Fee Description	Fee Paid
201	370	Utility filing fee	[ ]
206	165	Design Filing Fee	[ ]
207	255	Plant Filing Fee	[ ]
208	370	Reissue Filing Fee	[ ]
214	80	Provisional Filing Fee	[ ]

SUBTOTAL $

2. CLAIMS

			Extra Claims		Fee	Fee Paid
Total Claims	[ ]	- 20** =	[ ]	x	$ 9 =	[ ]
Independent Claims	[ ]	- 3** =	[ ]	x	42 =	[ ]
Multiple Dependent Claims				+	140 =	[ ]

***or number previously paid, if greater;*

SUBTOTAL $

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Fee Code	Fee Paid	Fee Description	Fee Paid
205	65	Surcharge - late filing fee or oath	[ ]
227	25	Surcharge - late provisional filing fee or cover sheet	[ ]
139	130	Non-English specification	[ ]
147	2,520	For filing a request for reexamination	[ ]
112	920	Requesting publication of SIR prior to Examiner action	[ ]
113	1,840*	Requesting publication of SIR after Examiner action	[ ]
215	55	Extension for reply within first month	[ ]
216	200	Extension for reply within second month	[200.00]
217	460	Extension for reply within third month	[ ]
218	720	Extension for reply within fourth month	[ ]
228	980	Extension for reply within fifth month	[ ]
219	160	Notice of Appeal	[ ]
220	160	Filing a brief in support of an appeal	[ ]
221	150	Request for Oral Hearing	[ ]
138	1,510	Petition to institute a public use proceeding	[ ]
240	55	Petition to revive -unavoidable	[ ]
241	640	Petition to revive - unintentional	[ ]
242	640	Utility issue fee (or reissue)	[ ]
243	230	Design issue fee	[ ]
244	310	Plant issue fee	[ ]
122	130	Petitions to the Commissioner	[ ]
123	50	Processing fee under 37 CFR 1.17(q)	[ ]
126	180	Submission of Information Disclosure Statement	[ ]
581	40	Recording each patent assignment per property (times number of properties)	[ ]
246	370	Filing a submission after final rejection (37 CFR .129(a))	[ ]
249	370	For each additional invention to be examined (37 CFR 1.129(b))	[ ]
279	370	Request for Continued Examination (RCE)	[ ]
169	900	Request for expedited examination of a design application	[ ]
195	300	Publication fee for early, voluntary, or normal publication	[ ]
196	300	Publication fee for republication	[ ]
089	200	Filing an application for patent term adjustment	[ ]
090	400	Request for reinstatement of term reduced	[ ]
Other fee (specify)			[ ]

* Reduced by Basic Filing Fee Paid **SUBTOTAL** $200.00

SUBMITTED BY				Complete (if applicable)	
NAME AND REG. NUMBER	Barbara G. Ernst, Reg. No. 30,377				
SIGNATURE	Barbara G. Ernst	DATE	October 11, 2002	DEPOSIT ACCOUNT USER ID	